

**WHAT IS CLAIMED IS:**

1                   1. A method for enhancing delivery of a compound into and across an  
2 animal ocular tissue, the method comprising:  
3                   administering to the ocular tissue a conjugate comprising the compound and a  
4 delivery-enhancing transporter,

5                   wherein:

6                   i. the compound is attached to the delivery-enhancing transporter  
7 through a linker, and

8                   ii. the delivery-enhancing transporter comprises fewer than 50 subunits  
9 and comprises at least 5 guanidino or amidino moieties, thereby increasing delivery of the  
10 conjugate into the ocular tissue compared to delivery of the compound in the absence of the  
11 delivery-enhancing transporter.

1                   2. The method of claim 1, wherein delivery of the conjugate into the  
2 ocular tissue is increased at least two-fold compared to delivery of the compound in the  
3 absence of the delivery-enhancing transporter.

1                   3. The method of claim 1, wherein delivery of the conjugate into the  
2 ocular tissue is increased at least ten-fold compared to delivery of the compound in the  
3 absence of the delivery-enhancing transporter.

1                   4. The method of claim 1, wherein the ocular tissue is one or more layers  
2 of epithelial or endothelial tissue.

1                   5. The method of claim 1, wherein the ocular tissue is the retina.

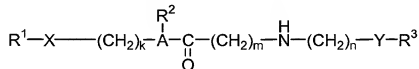
1                   6. The method of claim 1, wherein the ocular tissue is the optic nerve.

1                   7. The method of claim 1, wherein the linker is a releasable linker.

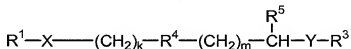
1                   8. The method of claim 7, wherein the linker is stable in a saline solution a  
2 pH 7 but is cleaved when transported into a cell.

1 9. The method of claim 1, wherein the subunits are amino acids.

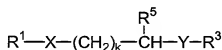
1 10. The method of claim 1, wherein the conjugate has a structure selected  
2 from the group consisting of structures 3, 4, or 5, as follows:



3 3



4 4



5 5

7 wherein:

8  $\text{R}^1$  comprises the compound;

9 X is a linkage formed between a functional group on the biologically active  
10 compound and a terminal functional group on the linking moiety;

11 Y is a linkage formed from a functional group on the transport moiety and a  
12 functional group on the linking moiety;

13 A is N or CH;

14  $\text{R}^2$  is hydrogen, alkyl, aryl, acyl, or allyl;

15  $\text{R}^3$  comprises the delivery-enhancing transporter;

16  $\text{R}^4$  is S, O,  $\text{NR}^6$  or  $\text{CR}^7\text{R}^8$ ;

17  $\text{R}^5$  is H, OH, SH or  $\text{NHR}_6$ ;

18  $\text{R}^6$  is hydrogen, alkyl, aryl, acyl or allyl;

19 k and m are each independently selected from 1 and 2; and  
20 n is 1 to 10.

1 11. The method of claim 10, wherein X is selected from the group  
2 consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-,  
3 -SO<sub>2</sub>NH-, -SONH-, phosphate, phosphonate phosphinate, and CR<sup>7</sup>R<sup>8</sup>, wherein R<sup>7</sup> and R<sup>8</sup> are  
4 each independently selected from the group consisting of H and alkyl.

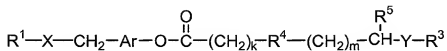
1 12. The method of claim 10, wherein the conjugate comprises structure 3, Y  
2 is N, and R<sup>2</sup> is methyl, ethyl, propyl, butyl, allyl, benzyl or phenyl.

1 13. The method of claim 10, wherein R<sup>2</sup> is benzyl; k, m, and n are each 1,  
2 and X is -OC(O)-.

1 14. The method of claim 10, wherein the conjugate comprises structure 4;  
2 R<sup>4</sup> is S; R<sup>5</sup> is NHR<sup>6</sup>; and R<sup>6</sup> is hydrogen, methyl, allyl, butyl or phenyl.

1 15. The method of claim 10, wherein the conjugate comprises structure 4;  
2 R<sup>5</sup> is NHR<sup>6</sup>; R<sup>6</sup> is hydrogen, methyl, allyl, butyl or phenyl; and k and m are each 1.

1 16. The method of claim 1, wherein the conjugate comprises structure 6 as  
2 follows:



3 6

4 wherein:

5 R<sup>1</sup> comprises the compound;

6 X is a linkage formed between a functional group on the biologically  
7 active compound and a terminal functional group on the linking moiety;

8 Y is a linkage formed from a functional group on the transport moiety  
9 and a functional group on the linking moiety;

10 Ar is an aryl group having the attached radicals arranged in an *ortho* or  
11 *para* configuration, which aryl group can be substituted or unsubstituted;  
12 R<sup>3</sup> comprises the delivery-enhancing transporter;  
13 R<sup>4</sup> is S, O, NR<sup>6</sup> or CR<sup>7</sup>R<sup>8</sup>;  
14 R<sup>5</sup> is H, OH, SH or NHR<sub>6</sub>;  
15 R<sup>6</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;  
16 R<sup>7</sup> and R<sup>8</sup> are independently selected from hydrogen or alkyl; and  
17 k and m are each independently selected from 1 and 2.

1 17. The method of claim 16, wherein X is selected from the group  
2 consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-,  
3 -SO<sub>2</sub>NH-, -SONH-, phosphate, phosphonate phosphinate, and CR<sup>7</sup>R<sup>8</sup>, wherein R<sup>7</sup> and R<sup>8</sup> are  
4 each independently selected from the group consisting of H and alkyl.

1 18. The method of claim 16, wherein R<sub>4</sub> is S; R<sup>5</sup> is NHR<sup>6</sup>; and R<sup>6</sup> is  
2 hydrogen, methyl, allyl, butyl or phenyl.

1 19. The method of claim 1, wherein the conjugate comprises at least two  
2 delivery-enhancing transporters.

1 20. The method of claim 1, wherein the conjugate is administered as an eye  
2 drop.

1 21. The method of claim 1, wherein the conjugate is administered as an  
2 injection.

1 22. The method of claim 1, wherein the delivery-enhancing transporter  
2 comprises a non-peptide backbone.

1 23. The method of claim 1, wherein the delivery-enhancing transporter is  
2 not attached to an amino acid sequence to which the delivery enhancing transporter molecule  
3 is attached in a naturally occurring protein.

1                   24. The method of claim 1, wherein the delivery-enhancing transporter  
2 comprises from 5 to 25 guanidino or amidino moieties.

1                   25. The method of claim 24, wherein the delivery-enhancing transporter  
2 comprises between 7 and 15 guanidino moieties.

1                   26. The method of claim 24, wherein the delivery-enhancing transporter  
2 comprises at least 6 contiguous guanidino and/or amidino moieties.

1                   27. The method of claim 1, wherein the delivery-enhancing transporter  
2 consists essentially of 5 to 50 amino acids, at least 50 percent of which amino acids are  
3 arginines or analogs thereof.

1                   28. The method of claim 27, wherein the delivery-enhancing transporter  
2 comprises 5 to 25 arginine residues or analogs thereof.

1                   29. The method of claim 28, wherein at least one arginine is a D-arginine.

1                   30. The method of claim 29, wherein all of the arginines are D-arginines.

1                   31. The method of claim 27, wherein at least 70 percent of the amino acids  
2 that comprise the delivery-enhancing transporter are arginines or arginine analogs.

1                   32. The method of claim 27, wherein the delivery-enhancing transporter is  
2 seven contiguous D-arginines.

1                   33. The method of claim 1, wherein the compound is a therapeutic for a  
2 disease selected from the group consisting of bacterial infections, viral infections, fungal  
3 infections, glaucoma, anterior, intermediate, and posterior uveitis, optic neuritis, Leber's  
4 neuroretinitis, retinitis, pseudotumor/myositis, orbital myositis, hemangioma/lymphangioma,  
5 toxocariasis, behcet's panuveitis, inflammatory chorisretinopathies, vasculitis, dry eye  
6 syndrome (Sjogren's syndrome), corneal edema, accommodative esotropia, cycloplegia,  
7 mydriasis, reverse mydriasis, and macular degeneracy.

1                   34. The method of claim 1, wherein the compound is selected from the  
2 group consisting of anti-bacterial compounds, anti-viral compounds, anti-fungal compounds,  
3 anti-protozoan compounds, anti-histamines, compounds that dilate the pupil, anesthetic  
4 compounds, steroidal antiinflammatory agents, antiinflammatory analgesics,  
5 chemotherapeutic agents, hormones, anticataract agents, neovascularization inhibitors,  
6 immunosuppressants, protease inhibitors, aldose reductase inhibitors, corticoid steroids,  
7 immunosuppressives, cholinergic agents, anticholinesterase agents, muscaric antagonists,  
8 sympathomimetic agents,  $\alpha$  and  $\beta$  adrenergic antagonists, and anti-angiogenic factors.

1                   35. The method of claim 34, wherein the compound is selected from the  
2 group consisting of acyclovir and cyclosporins.

1                   36. The method of claim 1, wherein the compound is transported across the  
2 blood-brain barrier.